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EXAMINER	
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1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,141	BRUNHAM ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,30,33,35 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,30,33,35 and 36* is/are rejected.

7)☒ Claim(s) *11 and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment to the claims filed 3/11/2008 has been entered into the record. Claims 16-29,31,32,34,37 and 38 are cancelled. Claims 1-15, 30,33,35 and 36 are pending and under examination

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

The drawings in this application filed 5/19/2006 have been accepted. No further action by Applicant is required.

Specification

The specification is objected to for the following minor informalities:

On p. 2 second to the last paragraph line 3 cysteine is misspelled.

On p. 4 second to the last paragraph line 10, Chlamydia is misspelled.

Applicants' cooperation is requested in checking and correcting any words that are not spelled correctly elsewhere in the application.

Election/Restrictions

Applicant's election of Group I and drawn to a nucleic acid molecule comprising a nucleic acid sequence which encodes the polypeptides SEQ ID NO: 2 and 6 and a nucleic acid molecule comprising a nucleic acid sequence SEQ ID NO: 1 and SEQ ID NO: 5, with traverse in reply to the restriction requirement filed 1/11/008 is acknowledged. The traversal is on the

ground(s) that the WO 02/14516 reference does not anticipate the originally filed claims nor the claims as amended.

This is not found persuasive. The amended claims still lack unity of invention in view of the art rejections of record. The groups of inventions as listed in the restriction requirement mailed 1/11/08 (see p. 2-4) still lack unity because Murdin et al. (WO 00/55326, Sept. 2000) anticipates the technical feature of the first appearing invention. The technical feature of the first appearing invention is anticipated by Murdin et al. Murdin et al teach a nucleic acid molecule comprising a nucleic acid sequence which encodes the instant SEQ ID NO:2. Further the instant nucleic acid sequence set forth SEQ ID NO:1 which encodes SEQ ID NO:2 does not share the technical feature (i.e. nucleic acid sequence) of the non-elected invention i.e. claims drawn to the nucleic acid sequence set forth in SEQ ID NO: 3 which encodes the amino acid sequence set forth in SEQ ID NO:4 (see Groups II-XII in p. 2-4 of the 1/11/08 restriction requirement),

The requirement is still deemed proper and is therefore made FINAL.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See Miller v. Eagle Mfg. Co., 151 U.S. 186 (1894); In re Ockert, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-15 and 30 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-15 and 30 of copending Application No.10/580142 ('142).
The instant claims are drawn to:
1) Claim 1 and dependent claims: a nucleic acid sequence which encodes a polypeptide selected group consisting of: (a) SEQ ID No: 2; b)
SEQ ID No: 6; (c)(an immunogenic fragment comprising at
least 12 consecutive amino acids from a polypeptide of (a) (b)or (c); and, (d) a polypeptide of (a), (b), or (c) which has been modified by conservative amino acid substitution without loss of immunogenicity, wherein said modified polypeptide is at least 75% identical in amino acid sequence to the corresponding polypeptide of (a), (b), or (c).
2) Claim 8 and dependent claims: a vector comprising a nucleic acid sequence which encodes a polypeptide selected group consisting of: (a) SEQ ID No: 2; b)
SEQ ID No: 6; (c)(an immunogenic fragment comprising at
least 100 consecutive amino acids from a polypeptide of (a) (b)or (c); and, (d) a polypeptide of (a), (b), or (c) which has been modified by conservative amino acid substitution without loss of

immunogenicity, wherein said modified polypeptide is at least 90% identical in amino acid sequence to the corresponding polypeptide of (a), (b), or (c).

3) Claim 30, An isolated polynucleotide from a strain of Chlamydia selected from the group consisting of:(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5; (c) a polynucleotide that is at least 95% homologous to the nucleotide sequence of SEQ ID NO: 1 or 5; and(d) a polynucleotide which hybridizes under stringent hybridizing conditions of 6xSSC containing 50% formamide at 42.degree. C. with a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 or 5, or 7 wherein administration to a mammal, induces an immune response in said mammal against infection by said strain of Chlamydia.

The '142 claims is drawn to the same invention as 1-3 above.

The '142 claims discloses:

1) Claim 1 and dependent claims: a nucleic acid sequence which encodes a polypeptide selected group consisting of: (a) SEQ ID No: 2; b)

SEQ ID No: 6; (c)(an immunogenic fragment comprising at

least 12 consecutive amino acids from a polypeptide of (a) (b)or (c); and, (d) a polypeptide of (a), (b), or (c) which has been modified by conservative amino acid substitution without loss of immunogenicity, wherein said modified polypeptide is at least 75% identical in amino acid sequence to the corresponding polypeptide of (a), (b), or (c).

2) Claim 8 and dependent claims: a vector comprising a nucleic acid sequence which encodes a polypeptide selected group consisting of: (a) SEQ ID No: 2; b)
SEQ ID No: 6; (c)(an immunogenic fragment comprising at
least 100 consecutive amino acids from a polypeptide of (a) (b)or (c); and, (d) a polypeptide of (a), (b), or (c) which has been modified by conservative amino acid substitution without loss of immunogenicity, wherein said modified polypeptide is at least 90% identical in amino acid sequence to the corresponding polypeptide of (a), (b), or (c).

3) Claim 30: An isolated polynucleotide from a strain of Chlamydia selected from the group consisting of:(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5; (c) a polynucleotide that is at least 95% homologous to the nucleotide sequence of SEQ ID NO: 1 or 5; and(d) a polynucleotide which hybridizes under stringent hybridizing conditions of 6xSSC containing 50% formamide at 42.degree. C. with a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 or 5, or 7 wherein administration to a mammal, induces an immune response in said mammal against infection by said strain of Chlamydia.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Objections

Claims 11 and 30 are objected to because of the following informalities:

Claim 11, line 2, pharmaceutically is misspelled.

Claim 30, line 8, please cancel SEQ ID NO: 3 and 7 because SEQ ID NO:3 and SEQ ID NO: 7 have been cancelled.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 30 and 33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims as written read on a Chlamydia microorganism which is a product of nature. The instant sequences exist in nature within said Chlamydia and conservative amino acid substitutions occur naturally in nature.

Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. The recitation of isolated or purified to distinguish the instant nucleic acids from that found in nature will obviate this issue.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15, 30,33,35 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to

1) Claim 1 and dependent claims: a nucleic acid sequence which encodes a polypeptide selected group consisting of: (a) SEQ ID No: 2; b)
SEQ ID No: 6; (c)(an immunogenic fragment comprising at
least 12 consecutive amino acids from a polypeptide of (a) (b)or (c); and, (d) a polypeptide of (a), (b), or (c) which has been modified by conservative amino acid substitution without loss of immunogenicity, wherein said modified polypeptide is at least 75% identical in amino acid sequence to the corresponding polypeptide of (a), (b), or (c).

2) Claim 8 and dependent claims: a vector comprising a nucleic acid sequence which encodes a polypeptide selected group consisting of: (a) SEQ ID No: 2; b)
SEQ ID No: 6; (c)(an immunogenic fragment comprising at
least 100 consecutive amino acids from a polypeptide of (a) (b)or (c); and, (d) a polypeptide of (a), (b), or (c) which has been modified by conservative amino acid substitution without loss of immunogenicity, wherein said modified polypeptide is at least 90% identical in amino acid sequence to the corresponding polypeptide of (a), (b), or (c).

3) Claim 30: An isolated polynucleotide from a strain of Chlamydia selected from the group consisting of:(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;(b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5; (c) a polynucleotide that is at least 95% homologous to the nucleotide sequence of SEQ ID NO: 1 or 5; and(d) a polynucleotide which hybridizes under stringent hybridizing conditions of 6xSSC containing 50% formamide at 42.degree. C. with a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 or 5, or 7 wherein administration to a mammal, induces an immune response in said mammal against infection by said strain of Chlamydia.

4) Claim 33 and dependent claims: a vaccine comprising a nucleic acid molecule encoding a polypeptide selected from any one of: (a) SEQ ID No: 2; b)
SEQ ID No: 6; (c) an immunogenic fragment comprising at
least 100 consecutive amino acids from a polypeptide of (a) (b)or (c); and, (d) a polypeptide of

(a), (b), or (c) which has been modified by conservative amino acid substitution without loss of immunogenicity, wherein said modified polypeptide is at least 90% identical in amino acid sequence to the corresponding polypeptide of (a), (b), or (c) wherein the nucleic acid molecule is either operatively linked to one or more control sequences for expression of the polypeptide in a mammalian or a bacterial cell, wherein the vaccine provides an immune response protective against disease caused by Chlamydia.

The claims are drawn to a large and variant genus of nucleic acid molecules comprising a nucleic acid sequence which encodes an immunogenic fragment comprising at least any 12 or 100 consecutive amino acids from SEQ ID NO: 2 or Seq ID NO: 6. The claims are also drawn to a large and variant genus of nucleic acids comprising a nucleic acid sequence which encodes a polypeptide with the amino acid sequence set forth in SEQ ID NO: 2 or 6 or any 12 or 100 consecutive amino acids from SEQ ID NO: 2 or SEQ ID NO: 6, which have been modified by amino acid substitution, wherein said modified polypeptide is at least 75% identical or 90% identical to SEQ ID NO: 2 or 6 or said immunogenic fragments. See claims 1, 8 and 10, for example. The claims are also drawn to a large and variant genus of nucleic acids comprising a at least any 38 consecutive nucleotides of SEQ ID NO: 1 or SEQ ID NO:5 and a polynucleotide that is at least 95% homologous to the nucleotide sequence of SEQ ID NO; 1 or 5 and any polynucleotide which hybridizes under stringent conditions with a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 or SEQ ID NO: 5.

The specification is devoid of any description (e.g. by common structure) of a representative number of species present in the variant genus of nucleic acid molecules comprising a nucleic acid sequence which encodes an immunogenic fragment comprising at least any 12 or any 100 consecutive amino acids from SEQ ID NO: 2 or Seq ID NO: 6. The specification does not teach the immunogenic epitopes of SEQ ID NO: 2 and SEQ ID NO: 6 and nucleic acids encoding said epitopes (SEQ ID NO: 6 is SEQ ID NO:2 but without the peptide

signal sequence, see p. 6 figure 1). Said variant genus is composed of members comprising nucleic acid sequences encoding different fragments with varying lengths and varied structure. The specification does not describe the common structure of this large genus of differing nucleic acids that is responsible for immunogenicity or acts as a vaccine that provides an immune response that is protective against disease caused by Chlamydia. Similarly, the specification does not teach the common structure of the large and variant genus of nucleic acid molecules comprising any 38 or more consecutive nucleotides of the nucleotide sequence set forth in SEQ ID NO: 1 or SEQ ID NO: 5 that is responsible for function of as a vaccine. The disclosure of the nucleotide sequences set forth in SEQ ID NO: 1 or SEQ ID NO: 5 and the amino acid sequence of the proteins the encode – SEQ ID NO: 2 and SEQ ID NO: 6, is not sufficient to describe the large and variant genus of nucleic acids molecules as claimed.

As to the claimed nucleic acid molecules that encode a polypeptide that is modified by conservative amino acid substitutions with at least 75% or at least 90% identical in amino acid sequence to the parent polypeptide as set forth in the claims, the claims are also drawn to a large and variant genus of nucleic acid molecules that encode a polypeptide that differ in at least 25% or at least any 10% of the polypeptides set forth in the claims. The instant specification does not teach which amino acids e.g. which 25% or 20% or 15% or 5% or 3%-1% of SEQ ID NO: 2 or 6 or fragments as set forth in the claims can be changed and still maintain the immunogenicity of said polypeptides or the nucleic acids encoding them. The specification does not teach the common structure of said large and variant genus responsible for the immunogenicity or induction of an immune response that is protective against disease caused by Chlamydia. As to conservative amino acid substitutions, the specification does not teach which

amino acid residue and in which part of the sequence set forth in Seq ID NO; 2 or SEQ ID NO: 6 or fragments as set forth in the claims can be conservatively replaced without loss of immunogenicity. Conservative amino acid substitutions at a particular residue position in a protein can drastically affect the structure and function of that protein (Simonida et al. The Journal of Neuroscience 10:117-124, 1990 p. 119 column 2 2nd full paragraph).

Thus, the disclosure of the amino acid sequences of SEQ ID NO:2 and SEQ ID NO:6 without description of the critical residues responsible for immunogenicity and which residues can be changed without loss of immunogenicity is insufficient description of the large and variant genus of conservative variants of SEQ ID NO: 2 or SEQ ID NO: 6 or fragments thereof.

As to polynucleotides that are 95% homologous to the nucleotide sequence of SEQ ID NO: 1 or Seq ID NO: 5 there is no description of sequences that are 95% homologous to SEQ ID NO; 1 or SEQ ID NO: 5 that function to induce an immune response against infection by Chlamydia. The genus of polynucleotides comprising nucleic acids that are at least 95 % homologous to SEQ ID NO: 1 or 5 is large and variant. The specification teaches on p. 9 that homology is established by sequence identity. The specification does not teach which 5% or less of SEQ ID NO; 1 or SEQ ID NO: 5 can be changed and still maintain the ability to induce an immune response against infection by Chlamydia. There is no common structure or function of said genus and a correlation of said common structure with the recited function. Similar analysis applied for a polynucleotide which hybridizes with a polynucleotide comprising the nucleotide sequence of SEQ ID NO: 1 or 5. The genus of polynucleotides which hybridize to SEQ ID NO: 1 or 5 encompasses variants of Seq ID NO: 1 or 5 and as set forth above, the specification does

not teach which parts of the nucleotide sequence set forth in SEQ ID NO: 1 or 5 and yield a polynucleotide that induces an immune response against Chlamydia infection.

As to the use of the above nucleic acid variants as a vaccine, the specification teaches that SEQ ID NO:1 (nucleic acid) encoding the protein whose amino acid sequence is set forth in SEQ ID NO:2 or SEQ ID NO:5 (nucleic acid truncated version of SEQ ID NO:1) which encodes SEQ ID NO: 6 is therapeutic in that immunized mice lost less body mass and had reduced bacterial burden. The specification fails to provide written description of fragments comprising at least 12-mers of SEQ ID NO:2 or 75% or 90% variants of SEQ ID NO:2 that are effective as vaccine and have the same activity as the full length polypeptide of SEQ ID NO:2. The protein of SEQ ID NO:2 is 554 amino acids in length and comprises a significant number of 12mers or 100mer fragments. No fragment has been disclosed or described that is immunogenic and effective as a vaccine as claimed. No variant of SEQ ID NO:2 is described that has been modified without loss of immunogenicity. Thus, while SEQ ID NO:2 has been shown to be immunogenic, the B and T cell epitopes have not been described. The major immunodominant epitopes that are responsible for detection have not been described as such, the skilled artisan could not envision any 12mer or 100 mer of SEQ ID NO:2 that encompasses such protective epitopes that would be reasonably expected to be protective as claimed. The specification provides no guidance as to what amino acids can be changed and still provide a protective immune response against Chlamydia pneumoniae much less the genus of *Chlamydia (C. pneumoniae, C. psittaci, C. pecorum, C. trachomatis*) as claimed.

The dictionary definition of vaccine is "A prophylactic or therapeutic material containing antigens derived from one or more pathogenic organisms which, on administration to man or

animal, will stimulate active immunity and protect against infection with these or related organism (i.e. produce protective immunity)." (The Dictionary of Immunology, Herbert et al eds, Academic Press, 1995) would clearly realize the critical deficiency of this specification with respect to the claimed "vaccine strains". It is well established in the art that immunogenicity/antigenicity does not correlate with protection from infection. Chandrashekar et al (US Patent 6,248,329) teaches "… it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection.." (column 1, lines 35-42).

Antibody epitopes are characterized by the art as either continuous or discontinuous (see pages 23-25, 27-33, Harlow et al , Antibodies A Laboratory Manual, Cold Spring Harbor Laboratory Press Inc., 1988). The specification generally teaches that intact SEQ ID NO:2 generates and immune response that treats disease (i.e. reduces burden of infection and reduces weight loss). T cell epitopes are continuous peptide fragments of a polypeptide or antigen that have been processed by an accessory cell. The specification generally describes that one can screen for protective/therapeutic 12 mer or 100mer fragments of SEQ ID NO:2. The specification relies on generic teachings. While the art can conventionally scan for potential contiguous antibody epitopes using conventional art accepted algorithms (Greenbaum et al, Journal of Molecular Recognition, 20(2):75-82, 2007), these methods do not identify discontinuous epitopes which are identified by crystallization of antibody/antigen complexes. The quality of the methods for B cell epitope prediction was widely considered to be too poor to be employed as a reliable tool by immunologists (paragraph spanning pages 75-82).

Furthermore, these methods also do not identify those epitopes contained in SEQ ID NO: 2 or 6 that are conserved in homologous polypeptides. The art recognizes that defining epitopes is not easy and there is a confusing divergence between the textbook definition of epitope and the definition that is in use in published descriptions of experimental investigations and that epitopes must be empirically determined (Greenspan et al, Nature Biotechnology 17:936-937, 1999). The specification clearly lacks description of any particular antibody epitope (i.e. antigenic determinant), either continuous or discontinuous that is within SEQ ID NO:2 or 6, either T cell or B cell that is within a 12mer or 100mer fragment of SEQ ID NO:2 that is immunogenic and protective. These particular characteristics of the B or T cell epitope is required by the definition of "vaccine". Applicants clearly did not provide written description of any particular antibody-binding or T-cell binding epitope contained in SEQ ID NO:2 or 6 that forms a part or all of an immunogenic fragment comprising a 12mer or 100mer, which necessarily functions therapeutically as a vaccine. While one could envision many 12mers or 100mers contained in SEQ ID NO:2 or 6 or 75% or 90% variants of SEQ ID NO:2 or 6, the skilled artisan would not be able to immediately envision which one of the hundreds are "immunogenic" and function as a vaccine. Even if the skilled artisan described an epitope, the presence of an epitope in a peptide (12mer or 100 mer) does not tell the skilled artisan about the ability of said epitope to provide for protection from infection. It is well established in the art that the use of peptide immunogens carries the problem, that antibodies raised against the peptide may not recognize the native antigen and that the percentage of antibodies raised against peptides that will bind to the native protein will vary from antigen to antigen (Harlow et al , Antibodies, A Laboratory Manual, Cold Spring Harbor Press, Inc. 1988, page 72). The specification does not describe any 12 mers or

100mer or variants that induce an immune response wherein the immune response binds the native antigen and that the immune response is immunoprotective. The fact that one could screen for epitopes and antigenic fragments is not the standard for written description. The specification lacks written description of any fragment or variant as claimed that provides the requisite functions of a vaccine. The specification does not provide sufficient guidance as to which of the amino acids may be changed "without loss of immunogenicity" while structural or functional activity (i.e. the instant vaccine) and specificity is retained. For example, Colman et al. (Research in Immunology 145: 33-36, 1994, p.33 column 2) disclose that a single amino acid changes in an antigen can effectively abolish the interaction with an antibody entirely. The specification provides no guidance as to what amino acids can be changed and still provide a protective immune response against Chlamydia pneumoniae . Finally, Houghten et al. (New Approaches to Immunization, Vaccines 86, Cold Spring Harbor Laboratory, p. 21-25, 1986) taught the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten et al. state (see page 24): "One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool." Finally, although the specification teaches that one could screen the courts have held that possession of a genus may not be shown by merely describing how to obtain members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895. The specification lacks

description of the specific structural features within the amino acid sequence set forth in SEQ ID NO:2 or 6 which correlate with protection from infection across the Chlamydia as claimed. Since the specification lacks description of the protective epitopes, the skilled artisan would not be able to immediately envision what 12mer or 100mer fragments of SEQ ID NO:2 or 6 would confer protection. Since the specification does not describe the genus of variants, the skilled artisan would not be able to readily envision what changes could be made and maintain the function of protection against infection. In view of the foregoing the specification lacks written description for immunoprotective (i.e. vaccine) fragments and 75% or 90% variants of SEQ ID NO:2 or 6 that act as vaccines.

Claims 1-3, 8-15 and 30, 33,35 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vaccine comprising a nucleic acid molecule comprising a nucleic acid sequence which encodes Seq ID NO: 1 or 5, wherein the vaccine reduces weight loss and reduces infection caused by Chlamydia trachomatis, does not reasonably provide enablement for a vaccine comprising nucleic acid molecule comprising a nucleic acid sequence which encodes fragments or conservative amino acid substituted variants or other variants of the amino acid sequence of SEQ ID NO: 2 or Seq ID NO: 6 as claimed; and does not provide enablement for a vaccine that protects against Chlamydia disease.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to the nucleic acid molecules and nucleic acids that are complementary to said nucleic acid molecules as set forth above (see written description rejection) used as a vaccine.

The specification teaches in experiments that mice immunized with SEQ ID NO: 1 (full length 60 kDa CRMP gene, 1662 bases) or SEQ ID NO: 5 (SEQ ID NO: 1 without the nucleic acid sequence encoding the signal sequence, 1554 bases) and challenged with Chlamydia trachomatis lost less body mass as compared to negative control and had lower lung titers of infection compared to control (p. 35-36 and figures 4 and 5).

However, the specification does not correlate the immunogenicity of other nucleic acids encoding an immunogenic fragment that comprises (a) 12 or more or 100 or more amino acids of SEQ ID NO: 2 or SEQ ID NO: 6 (proteins encoded by SEQ ID 1 or 5 respectively; (b) said polypeptide which has a conservative amino acid substitution and is at least 75% or 90% identical to said polypeptide with protection from Chlamydia infection or Chlamydia disease. The specification also does not correlate the immunogenicity of a (a) a nucleic acid molecule comprising 38 or more consecutive nucleotides of the nucleotide sequence set forth in SEQ ID NO: 1 or SEQ ID NO: 5 (b) or any other polynucleotide that is at least 95% homologous to SEQ ID NO: 1 or SEQ ID NO: 5 or any polynucleotide which hybridizes to SEQ ID NO: 1 or 5 with protection from Chlamydia infection or Chlamydia disease. As to a vaccine comprising a nucleic acid sequence complementary to the nucleic acid molecules as claimed in claim 1, such complementary nucleic acid sequence is antisense to the instant nucleic acid sequences. The specification does not correlate any immune response induced by nucleic acid sequences antisense to the nucleic acid sequences set forth in claim 1 with protection against infection or

protection from disease. Such antisense nucleic acid sequences would code for proteins different from the instant proteins and it is unpredictable that nucleic acids comprising said antisense nucleic acid sequence will induce an immune response against Chlamydia infection or disease.

The scope of Chlamydia comprises the species pneumoniae, pstitaci, trachomatis, percorum (specification p. 21). These species cause pneumonia and in the case of trachomatis cause pelvic inflammatory disease (Hartog et al Human Reproduction 19:1380-1384, 2004 and Roan et al Cellular Microbiology 10: 9-19, 2006 under introduction. Human diseases associated with Chlamydia infection are largely due to the inflammation and ensuing damage of infected tissues . The instant specification does not correlate an immune response induced by the instantly claimed vaccine with protection against disease caused by any of the Chlamydia species, diseases such as pneumonia or pelvic inflammatory disease. The specification does not correlate the reduction of weight loss or reduction of infection with any Chlamydia disease. In addition, the specification does not correlate an immune response generated by the nucleic acid molecules of the instant invention with protection against infection by Chlamydia species.

It is unpredictable that reduction of infection by dna vaccination with SEQ ID NO: 1 or SEQ ID NO: 5 will protect against disease caused by Chlamydia because the art teaches that if Chlamydia is not completely cleared by the immune system and persist within the host, repeated cycles of Chlamydia persistence alternating with reaction may stimulate chronic inflammation associated with Chlamydia induced disease (Roan et al, Cellular Microbiology (2008) 10:9-19, p. 14 column 2 under C. trachomatis persistence and immunopathology). In the instant case, though vaccination in the mice model reduces infection, the uncleared Chlamydia may still contribute to Chlamydial disease. Thus, more guidance or working example is needed to correlate reduction of

infection with protection from Chlamydial disease. Further, the specification does not teach whether the instant SEQ ID NO: 1 or SEQ ID NO: 5 is conserved in the other Chlamydia species. Thus, it is unpredictable that dna immunization with the instant Chlamydia nucleic acid molecules - SEQ ID NO: 1 or SEQ ID NO: 5 will protect against infection or disease caused by other species.

In view of the above, undue experimentation would be required of the skilled artisan to use the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 4, how can a nucleic acid sequence be complementary to a nucleic acid molecule? Does applicant mean the nucleic acid sequence is complementary to the nucleic acid sequence?

Claims 13-15 recite "the vaccine of claim 8 comprising a vaccine vector…". Claim 8 recites " A vaccine comprising a vector…".

It is not clear in claims 13-15 as written whether the vaccine in these claims comprises another vector different from the vector of claim 8. Clarification is requested in the claims.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 30 and 33 are rejected under 35 U.S.C. 102(b) as anticipated by Igietseme et al. Infection and Immunity p. 6798-6806, Dec. 2000.

The claims are drawn to a vaccine or immunogenic composition comprising a nucleic acid molecule comprising a nucleic acid sequence which encodes SEQ ID NO:2 or SEQ ID NO:6 or fragments of SEQ ID NO:2 or 6. The claims are also drawn to a vaccine or immunogenic composition comprising a nucleic acid molecule comprising SEQ ID NO:1 or 5 or fragments of SEQ ID NO:1 or 5

Igietseme et al teach a composition comprising *Chlamydia trachomatis* Serovar D (also see instant specification p. 34 last two sentences for the same Chlamydia) in a pharmaceutical acceptable carrier or diluent (PBS) (p. 6709 column 1 last paragraph. Said Chlamydia comprises a nucleic acid molecule comprising a nucleic acid sequence which encodes SEQ ID NO:2 or

SEQ ID NO:6 or nucleic acids comprising fragments of SEQ ID NO:2 or 6 and also comprises a nucleic acid molecule comprising SEQ ID NO:1 or 5 or nucleic acids comprising fragments of SEQ ID NO:1 or 5. Said composition is also immunogenic absent evidence to the contrary. The claims are drawn to the products not to the process of using the products as a vaccine.

Claims 1-7 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Murdin et al. WO 00/55326, Sept. 2000.

The claims are drawn to a vaccine comprising a nucleic acid sequence which encodes a polypeptide that is an immunogenic fragment comprising at least 12 consecutive amino acids from SEQ ID NO; 2 or SEQ ID NO: 6 and also drawn to a vaccine comprising a nucleic acid molecule comprising a nucleic acid sequence comprising at least 38 consecutive amino nucleotides of Seq Id NO: 1 or 5.

Murdin et al teach a nucleic acid molecule (SEQ ID NO:1 of Murdin et al) comprising a nucleic acid sequence which encodes a polypeptide (SEQ ID NO:2 of Murdin et al) comprising at least 12 consecutive amino acids of SEQ ID NO: 2 or SEQ ID NO: 6. See p. 53 claims 1 and 2 and the attached sequence alignment for the instant SEQ ID NO:2 (which comprises the instant SEQ ID NO:6). The polypeptide molecule of Murdin et al shares at least 12 consecutive amino acids with the instant polypeptides and the nucleic acid molecule of Murdin et al shares at least 38 consecutive nucleotides with the instant nucleic acid molecules – SEQ ID NO: 1 or SEQ ID NO: 5. Murdin et al teach a nucleic acid that is antisense (complementary) to the nucleic acid molecule of Murdin et al (see claim 3 p. 53). Murdin et al teach a nucleic acid molecule comprising said nucleic acid

molecule of Murdin et al which encodes at least 12 consecutive amino acids of the instant SEQ ID NO: 2 or SEQ ID NO: 6 and an additional polypeptide wherein the additional polypeptide is a heterologous signal sequence or wherein the additional polypeptide has adjuvant activity and also teach said nucleic acid molecule operatively linked to one or more expression control sequences (fusion protein, see claims 4-7). Said nucleic acid molecule will hybridize under stringent conditions of 6xSSC containing 50% formamide at 42oC with the instantly claimed SEQ ID NO: 1 or SEQ ID NO: 5 absent evidence to the contrary.

The recitation of the administration of the instantly claimed products to induce an immune response which protects against infection or disease caused by Chlamydia are intended use limitations which do not further limit the structure of the instant products. As the products of the prior art meets the structure of the instant claims, the products of the prior art would function similarly. The claims are drawn to the products not to the process of using the products as a vaccine.

Claims 1-2, and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Timms et al WO 200214516 A1 Feb. 2002 (cited in previous action)

Timms et al teach a nucleic acid molecule that comprises a nucleic acid sequence (SEQ ID NO: 23, OmcB/ompB gene of C. trachomatis MoPn) which encodes a polypeptide (SEQ ID NO: 24) selected from the instant SEQ ID NO: 2 or 6 (SEQ ID NO: 6 is a truncated version of SEQ ID NO: 2). See p. 13, p. 159-161 and the attached sequence alignment. SEQ ID NO: 24 of Timms et al comprises at least 12 or 100 consecutive

amino acids of the instant SEQ ID NO: 2 or 6 and SEQ ID NO: 23 of Timms et al comprises at least 38 consecutive nucleotides of the instant SEQ ID NO: 3 or 5.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-15, 30,33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Timms et al WO 200214516 A1 Feb. 2002 in view of Murdin et al. WO 00/55326, Sept. 2000.

Timm et al teach a nucleic acid molecule that comprises a nucleic acid sequence (SEQ ID NO: 23, OmcB/ompB gene of C. trachomatis MoPn) which encodes a polypeptide (SEQ ID NO: 24) selected from the instant SEQ ID NO: 2 or 6 (SEQ ID NO: 6 is a truncated version of SEQ ID NO: 2). See p. 13, p. 159-161 and the attached sequence alignment. SEQ ID NO: 24 of Timms et al comprises at least 12 or 100 consecutive amino acids of the instant SEQ ID NO: 2 or 6 and SEQ ID NO: 23 of Timms et al comprises at least 38 consecutive nucleotides of the instant SEQ ID NO: 3 or 5.

Timms et al does not teach said nucleic acid molecule encoding said polypeptide sequence as a fusion protein wherein the fusion protein comprises an additional polypeptide wherein the additional polypeptide is a heterologous signal peptide or wherein the additional polypeptide has adjuvant activity and does not teach a vector comprising said nucleic acid molecule or said nucleic acid in a carrier or diluent and does not teach said nucleic acid molecule operatively linked to one or more expression control sequences.

Murdin et al teach expression vector comprising a Chlamydia nucleic acid operatively linked to one or more expression control sequences in a vector so as to result in the expression of a fusion protein comprising the polypeptide encoded by said nucleic acid in addition to a heterologous signal polypeptide or a polypeptide that has adjuvant activity and thus enhances the immune response and teaches compositions of said vector in a carrier or diluent (see abstract, p. 19 lines 18-34 to p. 20, p. 22-25, p. 53-54 claims 1-11). Murdin et al teach that said vector when administered to a subject induces an immune response to Chlamydia trachomatis (p. 28 lines 18-30) and that the additional adjuvant polypeptide encoded by said vector enhances the

immune response to the Chlamydia protein expressed by the vector when administered (p. 54 claim 8). Murdin et al teach that

It would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to clone the nucleic acid molecule of Timms et al into the expression vector of Murdin et al and make a composition of the resultant vector in a carrier or diluent as taught by Murdin et al because Murdin et al teach that cloning a Chlamydia nucleic acid molecule into said expression vector and administering said vector in a carrier or diluent to a mammal infected with Chlamydia trachomatis induces an immune response to Chlamydia trachomatis and that additional adjuvant polypeptide encoded by said vector enhances the immune response to the expressed Chlamydia antigen.

Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Timms et al WO 200214516 A1 Feb. 2002 and Murdin et al. WO 00/55326, Sept. 2000 as combined as applied to claims 1-15, 30,33 and 35 further in view of Morein et al. Immunology and Cell Biology, 76:295-299, 1998.

The combination of Timms and Murdin is set forth supra. Said combination does not teach said composition comprising said vector further comprising an ISCOM adjuvant.

Morein et al teach ISCOMs act as adjuvants as wells as a delivery system for DNA antigens (see abstract and p. 296 column 1 line 8-10).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to add an ISCOM to the composition of Timms and Murdin as

combined as taught by Morein et al because Morein et al teach that ISCOMs acts as adjuvants and can act as a delivery system for DNA antigens.

Status of the Claims

Claims 1-15, 30,33,35 and 36 are rejected. Claims 11 and 30 are objected to.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the

examiner by telephone are unsuccessful, the examiner's Supervisory Examiner Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Oluwatosin Ogunbiyi/

Examiner, Art Unit 1645

/Patricia A. Duffy/

Primary Examiner, Art Unit 1645